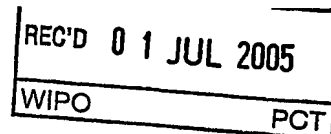


PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)



| | | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|--|---|-------------------------------------|-----------|----------------------|--------------------------|------------|----------|--------------------------|-------------|--|-------------------------------------|------------|----------------------------|-------------------------------------|-----------|---|--------------------------|------------|-------------------------|--------------------------|-------------|--|--------------------------|--------------|---|
| Applicant's or agent's file reference H1875 PCT S3 | FOR FURTHER ACTION See Form PCT/PEA/416 | | | | | | | | | | | | | | | | | | | | | | | | | |
| International application No. PCT/EP2004/007538 | International filing date (day/month/year) 08.07.2004 | Priority date (day/month/year) 08.07.2003 | | | | | | | | | | | | | | | | | | | | | | | | |
| International Patent Classification (IPC) or national classification and IPC C07J1/00 | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Applicant GLYCOMED SCIENCES LIMITED et al. | | | | | | | | | | | | | | | | | | | | | | | | | | |
| <ol style="list-style-type: none"> 1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36. 2. This REPORT consists of a total of 7 sheets, including this cover sheet. 3. This report is also accompanied by ANNEXES, comprising: <ol style="list-style-type: none"> a. <input type="checkbox"/> sent to the applicant and to the International Bureau a total of sheets, as follows: <ul style="list-style-type: none"> <input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions). <input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box. b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions). | | | | | | | | | | | | | | | | | | | | | | | | | | |
| <ol style="list-style-type: none"> 4. This report contains indications relating to the following items: <table style="width: 100%; border: none;"> <tr> <td style="width: 10%;"><input checked="" type="checkbox"/></td> <td style="width: 15%;">Box No. I</td> <td>Basis of the opinion</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. II</td> <td>Priority</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. III</td> <td>Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</td> </tr> <tr> <td><input checked="" type="checkbox"/></td> <td>Box No. IV</td> <td>Lack of unity of invention</td> </tr> <tr> <td><input checked="" type="checkbox"/></td> <td>Box No. V</td> <td>Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. VI</td> <td>Certain documents cited</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. VII</td> <td>Certain defects in the international application</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. VIII</td> <td>Certain observations on the international application</td> </tr> </table> | | | <input checked="" type="checkbox"/> | Box No. I | Basis of the opinion | <input type="checkbox"/> | Box No. II | Priority | <input type="checkbox"/> | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability | <input checked="" type="checkbox"/> | Box No. IV | Lack of unity of invention | <input checked="" type="checkbox"/> | Box No. V | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement | <input type="checkbox"/> | Box No. VI | Certain documents cited | <input type="checkbox"/> | Box No. VII | Certain defects in the international application | <input type="checkbox"/> | Box No. VIII | Certain observations on the international application |
| <input checked="" type="checkbox"/> | Box No. I | Basis of the opinion | | | | | | | | | | | | | | | | | | | | | | | | |
| <input type="checkbox"/> | Box No. II | Priority | | | | | | | | | | | | | | | | | | | | | | | | |
| <input type="checkbox"/> | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability | | | | | | | | | | | | | | | | | | | | | | | | |
| <input checked="" type="checkbox"/> | Box No. IV | Lack of unity of invention | | | | | | | | | | | | | | | | | | | | | | | | |
| <input checked="" type="checkbox"/> | Box No. V | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement | | | | | | | | | | | | | | | | | | | | | | | | |
| <input type="checkbox"/> | Box No. VI | Certain documents cited | | | | | | | | | | | | | | | | | | | | | | | | |
| <input type="checkbox"/> | Box No. VII | Certain defects in the international application | | | | | | | | | | | | | | | | | | | | | | | | |
| <input type="checkbox"/> | Box No. VIII | Certain observations on the international application | | | | | | | | | | | | | | | | | | | | | | | | |
| Date of submission of the demand 08.02.2005 | Date of completion of this report 30.06.2005 | | | | | | | | | | | | | | | | | | | | | | | | | |
| Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465 | Authorized Officer Telephone No. +49 89 2399- 7896 | | | | | | | | | | | | | | | | | | | | | | | | | |

**INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY**

International application No.
PCT/EP2004/007538

Box No. I - Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
- ☐ international search (under Rules 12.3 and 23.1(b))
 - ☐ publication of the international application (under Rule 12.4)
 - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages

1-15 as originally filed

Claims, Numbers

1-27 as originally filed

- ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing
3. ☐ The amendments have resulted in the cancellation of:
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
 - ☐ any table(s) related to sequence listing (*specify*):
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
 - ☐ any table(s) related to sequence listing (*specify*):

* If item 4 applies, some or all of these sheets may be marked "superseded."

**INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY**

International application No.
PCT/EP2004/007538

Box No. IV Lack of unity of invention

1. ☒ In response to the invitation to restrict or pay additional fees, the applicant has:
- ☐ restricted the claims.
 - ☒ paid additional fees.
 - ☐ paid additional fees under protest.
 - ☐ neither restricted nor paid additional fees.
2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is
- ☐ complied with.
 - ☒ not complied with for the following reasons:
see separate sheet
4. Consequently, this report has been established in respect of the following parts of the international application:
- ☒ all parts.
 - ☐ the parts relating to claims Nos. .

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

| | | |
|-------------------------------|-------------|------|
| Novelty (N) | Yes: Claims | 1-27 |
| | No: Claims | --- |
| Inventive step (IS) | Yes: Claims | --- |
| | No: Claims | 1-27 |
| Industrial applicability (IA) | Yes: Claims | 1-27 |
| | No: Claims | --- |

2. Citations and explanations (Rule 70.7):

see separate sheet

Re Item IV

Lack of unity of invention

This Authority considers that there are 2 inventions covered by the claims indicated as follows:

- I: Claim 1-22,24-27 : A process for the preparation of steroid derivatives bearing in position 3 a triose moiety as claimed in claim 1.
- II: Claim 24 : Two new compounds namely tomatidin-3-yl triose and demissidin-3-yl triose.

The reasons for which the inventions are not so linked as to form a single general inventive concept, as required by Rule 13.1 PCT, are as follows:

The subject-matter of claims 1-22,24-27 concerns a process for the preparation of (potentially) known compounds whereas the subject-matter of claim 23 concerns new compounds. Thus, the prior art must be considered under two different aspects as there are two different technical problems to be solved, hence resulting in a non-unity.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

- D1: LI C ET AL: "Synthesis of diosgenyl alpha-l-rhamnopyranosyl-(1->2)-[beta-d-glucopyranosyl-(1->3)]-beta-d-glucopyranoside (gracillin)" CARBOHYDRATE RESEARCH, ELSEVIER SCIENTIFIC PUBLISHING COMPANY. AMSTERDAM, NL, vol. 306, no. 1-2, January 1998 (1998-01), pages 189-195, XP004204799 ISSN: 0008-6215 (GLYCOMED SCIENCES LTD ; SHAHID MOHAMMED (GB)) 6 March 2003 (2003-03-06)
- D2: ZOU C-C ET AL: "The synthesis of gracillin and dioscin: two typical representatives of spirostanol glycosides" CARBOHYDRATE RESEARCH, ELSEVIER SCIENTIFIC PUBLISHING COMPANY. AMSTERDAM, NL, vol. 338,

no. 8, 4 April 2003 (2003-04-04), pages 721-727, XP004417407 ISSN: 0008-6215

- D3: IKEDA T ET AL: "Synthesis of neosaponins having an alpha-l-rhamnopyranosyl-(1->4)-[alpha-l-rhamnopyranosyl-(1->2)]-d-glucopyranosyl glyco-linkage" TETRAHEDRON LETTERS, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 42, no. 12, 18 March 2001 (2001-03-18), pages 2353-2356, XP004229921 ISSN: 0040-4039
- D4: WO 03/018604 A

- D5: WO 2005/005454 A (GLYCOMED SCIENCES LIMITED; LAWSON, CHRISTOPHER, JOHN; WEYMOUTH-WILSON,) 20 January 2005 (2005-01-20)
- D6: WO 2004/096830 A (GLYCOMED SCIENCES LIMITED; SHAHID, MOHAMMED) 11 November 2004 (2004-11-11)

D5 and D6 which are "E" documents not prior art according to the Chap II PCT proceedings.

Nevertheless, the extensive examination of that document, on the question whether it constitutes prior art or not, will depend essentially on the analysis of the claimed priority rights of the present application and will only be performed in the regional European proceedings to come.

Novelty of Invention 1 :

The subject-matter of the present application concerns the preparation of steroids bearing in position 3 a trisaccharidic moiety (saponins).

Since none of the available prior art discloses the claimed process, the subject-matter of invention 1 is considered new.

Inventive step of invention 1 :

D1, which is considered to represent the closest prior art, concerns the synthesis of saponins, consisting in synthetising the 1-->2 bond, then grafting the steroid and finally

synthetising the 1-->3 bond.

The subject-matter of present invention 1 mainly differs in that the 1-->2 bond is created, then steroid is grafted (and finally the 1-->2 bond is synthetised : see claim 12).

The problem to be solved can be regarded as providing an alternative process for the preparation of triose steroids.

in D1-D3, the coupling between the sugar part and the steroid is performed by reacting a steroid, an halo-glycoside and AgOTf, while in D4 an -S-Et glycoside may be used in combination with AgOTf. in every case a "similar" intermediate as the one depicted under Formula XIII (triflate intermediate) is obtained.

Thus, the subject-matter of claim 1 of invention 1 is merely considered as an adaptation of the prior art using a 1-->3 disaccharide (of formula XIII) instead of a 1-->2 disaccharide.

The claims 2-22 do not seem to contain particular features that a man skilled in the art could not perform either by knowing the cited prior art or with his general knowledge (in particular of protecting groups).

Thus, at present, the subject-matter of invention 1 is not considered inventive.

Novelty of Invention 2 :

The subject-matter invention 2 concerns tomatidin-3-yl and demissidin-3-yl derivatives bearing in position 3 a trisaccharidic moiety .

Since none of the available prior art discloses the claimed compounds, the subject-matter of invention 2 is considered new.

Inventive step of invention 2 :

As no use or activity or comparative tests, etc, are provided in the present application for the two claimed compounds of invention 2, is it not possible to formulate a problem to be solved by the compounds of invention 2.

**INTERNATIONAL PRELIMINARY
REPORT ON PATENTABILITY
(SEPARATE SHEET)**

International application No.

PCT/EP2004/007538

As new compounds are not patentable *per se*, no inventive step can be acknowledged for inventive 2.

Re Item VII

Certain defects in the international application

Claim 2 is dependant on itself instead of being dependant on claim 1 (Art. 6 PCT).